

Remarks

I. Support for the Amendments

Support for the foregoing amendments to the claims may be found throughout the specification. Specifically, support for the amendments to claims 14, 15, 19, 31, and 40 may be found in the specification at page 18, lines 4-9; at page 31, line 29, through page 33, line 23; and throughout the Examples. Hence, these amendments do not add new matter and their entry and consideration are respectfully requested.

II. Status of the Claims

By the forgoing amendments, claims 14, 15, 19, 31, and 40 have been amended. Claims 14-51, 65-76 and 81-104 are pending in the application, with claims 14, 19, 31 and 40 being the independent claims.

III. Summary of the Office Action

In the Office Action dated August 11, 2003, the Examiner has made four rejections of the claims. Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

IV. The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at pages 2-3, the Examiner has rejected claims 31-36, 40-51, 73-76, 83-84 and 87-88 under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants respectfully traverse this rejection.

The Examiner contends that the claims are vague and indefinite for failing to clearly recite how recombinational cloning is enhanced via the present invention. Applicants respectfully disagree with these contentions.

Present claim 31 (and hence, claims 32-36, 73-76, 83, and 87 that depend ultimately therefrom and that are also rejected) recites a method for enhancement of recombinational cloning of one or more desired nucleic acid molecules comprising: (a) forming a mixture by mixing *in vitro* one or more desired first nucleic acid molecules with one or more second nucleic acid molecules and with at least one ribosomal protein that enhances recombinational cloning and an effective amount of at least one recombination protein; and (b) incubating the mixture under conditions sufficient to transfer the one or more desired first nucleic acid molecules into one or more of the second nucleic acid molecules.

Present claim 40 (and hence, claims 41-51, 84, and 88 that depend ultimately therefrom and that are also rejected) recites a method for enhancement of recombinational cloning, comprising contacting at least a first nucleic acid molecule and at least a second nucleic acid molecule, each comprising at least one recombination site, *in vitro* with one or more ribosomal proteins that enhance recombinational cloning and with one or more recombination proteins to form a mixture, and incubating the mixture under conditions favoring the production of at least one product nucleic acid molecule.

Applicants submit that the ordinarily skilled artisan would readily recognize that the one or more ribosomal proteins are responsible for the enhancement of recombinational cloning recited in claims 31 and 40. Moreover, one of ordinary skill would readily understand the meaning of "enhancement" of recombinational cloning, particularly in view of the non-limiting examples of such enhancement disclosed in the Examples of the present

specification. Hence, Applicants contend the claims as currently presented clearly define the metes and bounds of the presently claimed invention, and therefore are not vague and indefinite.

In view of the forgoing remarks, Applicants respectfully request that the rejection of claims 31-36, 40-51, 73-76, 83-84 and 87-88 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

V. The Rejection Under 35 U.S.C. § 102(b) Over Nash

In the Office Action at pages 3-5, the Examiner has rejected claims 31-32, 36, 38-51, 65-72, 74-76, 87-89, 91-95, 98 and 100-103 under 35 U.S.C. § 102(b) as being anticipated by Nash (*Meth. Enzymol.* 100:210-216 (1983); hereinafter “Nash”). Applicants respectfully traverse this rejection.

The Examiner contends that Nash discloses the recombination of two DNA molecules via Int mediated recombination between *attL* and *attR* sites. The Examiner further contends that since the Int protein was purified from *E.coli* cells, it is inherent that the crude extracts used in Nash in the recombination reactions would include *E. coli* ribosomal proteins. Applicants respectfully disagree with these contentions.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984); see also *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996) (“[t]o anticipate a claim, a reference must disclose every element of the challenged claim and

enable one skilled in the art to make the anticipating subject matter.”). This burden is not met by Nash.

As noted above, present claim 31 (and hence, claims 32, 36, 38-39, 65-72, 74-76, 87, 89, 91-95, 98 and 100-103 that depend ultimately therefrom and that are also rejected over Nash) and present claim 40 (and hence, claims 41-51, 88-89, 91-95, 98 and 100-103 that depend ultimately therefrom and that are also rejected over Nash) both recite methods for enhancing recombinational cloning that comprise at least one ribosomal protein that enhances recombinational cloning. Applicants submit that Nash does not expressly disclose the use of ribosomal proteins, or the use of ribosomal proteins that enhance recombinational cloning. Apparently recognizing that Nash fails to expressly anticipate the presently claimed invention, the Examiner instead contends that Nash *inherently* discloses the invention. *See* Paper No. 28, at page 4. Applicants respectfully disagree with this contention, and wish to remind the Examiner that “[i]n order for a disclosure to be inherent . . . the missing descriptive matter must necessarily be present in the [cited reference] such that one skilled in the art would recognize such a disclosure.” *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998). In the present case, the Examiner has pointed to no disclosure in Nash that is “necessarily present” such that it would be recognized as by one of ordinary skill as disclosing the use of ribosomal. Hence, the Examiner’s attempted reliance upon inherent anticipation in the present case is factually and legally unfounded.

Applicants therefore respectfully submit that Nash does not expressly or inherently disclose every element of the presently claimed invention. Hence, in view of *Kalman*, the rejection of claims 31-32, 36, 38-51, 65-72, 74-76, 87-89, 91-95, 98 and 100-103 under

35 U.S.C. § 102(b) over Nash is in error; reconsideration and withdrawal therefore are respectfully requested.

VI. The Rejection Under 35 U.S.C. § 103(a) Over Hartley in View of Nash, Abremski I or Abremski II

In the Office Action at pages 5-9, the Examiner has rejected claims 14-51, 65-76 and 81-104 under 35 U.S.C. § 103(a) as being unpatentable over Hartley *et al.* (U.S. Patent No. 5,888,732; hereinafter "Hartley") in view of Nash, Abremski *et al.* (*J. Biol. Chem.* 259:1509-1514 (1984), document V cited on Form PTO-892 attached to Paper No. 8; hereinafter "Abremski I") or Abremski *et al.* (*J. Biol. Chem.* 257:9658-9662 (1982), document W cited on Form PTO-892 attached to Paper No. 8; hereinafter "Abremski II"). Applicants respectfully traverse this rejection.

Present claim 14 (and hence claims 15-18, 21-27, 29-30, 81, 85, and 89-104 that depend ultimately therefrom and that are also rejected), and present claim 19 (and hence claims 20, 28, 82, 86, and 89-103 that depend ultimately therefrom and that are also rejected) both recite methods for cloning or subcloning one or more desired nucleic acid molecules comprising at least one ribosomal protein that enhances recombinational cloning. As noted above, present claim 31 (and hence claims 32-39, 65-76, 83, 87, and 89-103 that depend ultimately therefrom and that are also rejected) and present claim 40 (and hence claims 41-51, 84, 88, and 89-103 that depend ultimately therefrom and that are also rejected) both recite methods for enhancement of recombinational cloning comprising at least one ribosomal protein that enhances recombinational cloning.

The Examiner notes that Hartley does not disclose the use of crude lysates comprising recombination factors and further notes that Hartley does not disclose the addition of ribosomal proteins to recombination reaction mixtures (*see* Office Action at page 6, second full paragraph). The Examiner attempts to supplement Hartley with the disclosures of Nash, Abremski I and/or Ambremski II, contending that the ordinarily skilled artisan would have been motivated to use the crude *E. coli* lysates disclosed in Nash, Abremski I, or Abremski II in the recombinational cloning methods disclosed in Hartley. The Examiner contends that the ordinarily skilled artisan would have been motivated to use such lysates “in order to receive the expected benefit of providing one or more recombination proteins without the need for further purification.” The Examiner further states that “[o]ne of skill in the art, aware of the pertinent art concerning *in vitro* site-specific recombination reactions would necessarily have been aware of the ability to use crude extracts of cells to provide essential recombination proteins to such *in vitro* recombination reactions.” The Examiner also contends that it is reasonable to expect that the crude extracts disclosed in Nash, Abremski I and/or Abremski II would have also contained ribosomal proteins.

Applicants respectfully disagree with these contentions, and incorporate by reference herein the remarks made in the Amendment and Reply submitted May 19, 2003, in response to the previous Office Action. Applicants also offer the following additional remarks regarding this rejection.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden

only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Specifically, there must be a reason, suggestion, or motivation in the cited art that would motivate one of ordinary skill to combine the references, and that would also suggest a reasonable likelihood of success in making or using the invention as claimed as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, the Examiner's burden has not been satisfied.

Applicants submit that the ordinarily skilled artisan would not have been motivated to combine the disclosure of Hartley with the disclosures of Nash, Abremski I and/or Abremski II to generate the presently claimed invention. The ordinarily skilled artisan, practicing the invention disclosed in Hartley, would not have been motivated to modify the methods of Hartley by incorporating the use of the crude extracts disclosed in Nash, Abremski I or Abremski II. None of the cited references provides any disclosure or suggestion that such modifications should be made. Absent such a suggestion, the ordinarily skilled artisan would not have been motivated to combine the references cited by the Examiner.

Applicants submit that in attempting to support this obviousness rejection, the Examiner appears to contend that it would have been obvious to the ordinarily skilled artisan to try the crude cell extracts disclosed in Nash, Abremski I or Abremski II in the methods disclosed in Hartley. However, the Examiner is reminded that whether a particular combination of elements might be obvious to try is not a legitimate test of patentability, and

therefore cannot support a rejection under 35 U.S.C. § 103. *See Amgen v. Chugai*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988); *In re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988); *In re Geiger*, 815 F.2d 686, 688 (Fed. Cir. 1987). When “what would have been ‘obvious to try’ would have been to . . . try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave . . . no direction as to which of many possible choices is likely to be successful,” it would not have been obvious to produce the claimed invention. *O'Farrell*, 853 F.2d at 903 (Fed. Cir. 1988). As noted above, the disclosure of Hartley provides no suggestion or motivation to use crude extracts such as those disclosed in the remaining cited references, and the “obvious to try” standard has been firmly and consistently rejected by the Federal Circuit.

Finally, Applicants note that the rejection over Nash under 35 U.S.C. § 102 (*see* Section V, hereinabove) was apparently based upon disclosure in that reference that may have been inherent. Presumably, this is the same disclosure in Nash relied upon by the Examiner in making the present rejection under 35 U.S.C. § 103. Applicants wish to remind the Examiner, however, that there is no such thing as “inherent obviousness,” since inherence and obviousness are different legal concepts. *See In re Spormann*, 150 USPQ 449, 452 (C.C.P.A. 1966). That which is inherent cannot be obvious, since inherent information “is not necessarily known [and] Obviousness cannot be predicated on what is unknown.” *Id.* Since the present rejection is based on obviousness, any contention by the Examiner that is based on the possible presence of inherent knowledge in Nash must necessarily fail.

In view of the forgoing remarks, Applicants respectfully submit that Hartley, Nash, Abremski I and/or Abremski II cannot be properly combined to create a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection of claims 14-51, 65-76 and 81-104 under 35 U.S.C. § 103(a) are respectfully requested.

VII. The Double Patenting Rejection

In the Office Action at pages 10-11, the Examiner has rejected claims 14-51, 65-76 and 81-104 under the judicially created doctrine of obviousness-type double patenting as being upatentable over claims 29-37 of Hartley in view of Nash or Abremski I or Abremski II. Applicants respectfully traverse this rejection.

As noted above, the presently claimed invention recites methods for cloning or subcloning nucleic acid molecules, and methods for enhancement of recombinational cloning of nucleic acid molecules, comprising at least one ribosomal protein that enhances recombinational cloning. For at least the reasons discussed in detail above (which are reiterated herein), Hartley does not disclose or suggest the use of ribosomal proteins that enhance recombinational cloning. For at least the reasons also discussed in detail above (which are also reiterated herein), the Examiner cannot properly supplement the teachings of Hartley with the disclosures of Nash, Abremski I or Abremski II, alone or in combination, as none of these secondary references expressly disclose the use of ribosomal proteins that enhance recombinational cloning (and since any inherent disclosure in these references is not properly used in an obviousness rejection). Hence, Applicants respectfully assert that the presently claimed invention is patentably distinct over the claims of Hartley, alone or in combination with Nash, Abremski I or Abremski II.

In view of the forgoing remarks, reconsideration and withdrawal of the obviousness-type double patenting rejection are respectfully requested.

VIII. Conclusion

All of the stated grounds of rejection have been properly traversed. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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